# DEVICE AND METHODOLOGY FOR OCULAR STIMULATION

## CROSS-REFERENCE TO RELATED APPLICATIONS:

This application claims priority from provisional patent application Serial No. 60/457,389 filed on March 24, 2003, which is incorporated herein by reference and made a part hereof.

## FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT:

Not Applicable.

## BACKGROUND OF THE INVENTION

Blindness can occur when any part of the vision system (the optics, the retina, the optic nerve or the visual cortex) are interrupted or destroyed. The leading cause of blindness in the developed world is Retinal Degeneration (RD). The two principle diseases resulting in RD are Age Related Macular Degeneration (AMD) and Retinitis Pigmentosa (RP). AMD is the leading cause of blindness in the developed world. According to a March 1997 review in the Optometry Journal, 10 percent of the U.S. population over the age of 52 has AMD and 33 percent of individuals over the age of 75 have AMD.

AMD can be categorized into two forms, a non-neovascular (dry, atrophic) form and a neovascular (wet, exudative) form. The non-neovascular form involves alterations of pigment distribution, loss of retinal pigment epithelium (RPE) cells and photoreceptors, and diminished retinal function due to an overall atrophy of the cells. The neovascular form of AMD involves proliferation of abnormal choroidal vessels, which penetrate the Bruch's membrane and RPE layer into the subretinal space forming extensive clots and scars. The cause of AMD is unknown.

RP is a name given to a large group of degenerative diseases. The dominant form of RP is associated with mutations in the visual pigment, rhodopsin protein. These mutations account for about 25 percent of RP cases in the U.S.

Normal retinal cell function is a photo-induced electrochemical reaction converting light energy into an electrical impulse. The photochemical reaction begins with the absorption of light by Rhodopsin. Rhodopsin breaks down into several intermediate compounds, but eventually forms metarhodopsin II (activated rhodopsin). This chemical causes electrical impulses that are transmitted via synapses to the first complex array of

interneurons (bipolar cells and horizontal cells). These in turn connect to the ganglion cells, whose axons form the optic nerve.

The same electrical impulse travels to the visual cortex of the brain via the optic nerve and results in a vision sensation. With AMD, RP and other Retinal Degenerative (RD) diseases, photoreceptor retinal cells atrophy and eventually lose cell function. Since the bipolar and horizontal cells no longer receive neuronal signals, the retinal interneuronal layers undergo remodeling or arborization. The neural network is "pruned" and refined by mechanisms that include cell death, selective growth, loss of neurites and elimination of synapses (Neely and Nicholls, 1995). This natural phenomenon is related to the adage: "use it or lose it."

It has been demonstrated that electrical stimulation of ganglion cells shows a rescue or neurotrophic effect, which promotes cell survival. Specifically, several studies performed on spiral ganglion cells show a survival due to electrical stimulation from cochlear implants (Leake et al., 1991; Leake et al., 1999). Recently documented studies of implanted human subjects with Microphotodiode Arrays (MPDA) have shown an overall improvement in vision. The results indicate that the MPDA in effect has not restored vision in the specific area in which the implant is placed; instead, results indicate a neurotrophic rescue effect due to the electrical stimulation on the remaining retinal cells.

The application of electrical stimulation to organ systems other than the ocular system is known to promote and maintain certain cellular functions. Electrical stimulation has been documented in bone growth and spinal cord growth, as well as in cochlear cell survival as mentioned earlier (Dooley et al., 1978; Evans et al., 2001; Kane, 1988; Koyama et al., 1997; Lagey et al., 1986; Politis and Zanakis, 1988a; Politis and Zanakis, 1988b; Politis and Zanakis, 1989; Politis et al., 1988a; Politis et al., 1988b). Electrical stimulation has also been applied in Deep Brain Stimulators for Parkinson's Disease and Essential Tremor. This electrical stimulation temporarily disables the overactive cells that cause Parkinson's disease symptoms (O'Suilleabhain P.E., 2003).

Electrical stimulation of the ocular system has been under study for several decades. As early as the 1890's, scientists have been experimenting with the use of an electric current to produce an artificial vision sensation or phosphene. Brindley's work in the 1950's documents the thresholds needed to induce such a phosphene (Brindley 1955). There are also numerous amounts of animal work that suggest that the retina responds to externally applied electrical stimulation (Kuras, A.V., Khusainovene NP. 1981, Knighton, R.W. 1975, Humayun, M.S. 2001, Grumet, A.E. et. al. 2001).

Tassicker described the notion of an implanted artificial vision device in a U.S. patent in 1956 (U.S. Patent 2,760,483). A light-sensitive selenium cell was placed behind

the retina of a blind patient and transiently restored the patient's ability to perceive a sensation of light. Since then, several groups have been working to develop a device that can be implanted in place of the degrading photoreceptors. These groups attempt to restore vision by using photonic properties of semiconductors designed to mimic the electric charge that damaged retinal cells would otherwise generate. However, there are few devices or treatments available that can slow, stop or reverse retinal degeneration.

Recent studies of the electrical stimulation of the cut optic nerve show a survival of axotomized retinal ganglion cells in vivo. The conclusion from this experimentation demonstrates that electrical stimulation of the optical nerve enhances the survival of axotomized retinal ganglion cells in vivo due to electrical activation of their soma (Morimoto T., 2002).

These findings led me to find a means for providing electrical stimulation to a diseased eye in a minimally invasive manner, to stimulate the regrowth, rescue and survival of ocular neural tissue and the entire ocular system for the treatment of blinding diseases such as Retinitis Pigmentosa, Age Related Macular Degeneration, and other Retinal Degenerative diseases.

## SUMMARY OF THE INVENTION

It is an advantage of the present invention to provide novel methods and apparatus for treating various diseases including Retinitis Pigmentosa and Age Related Macular Degeneration. Further, the present invention provides a device including a contact lens with a member embedded in a surface thereof for electrically stimulating an eye of a wearer of the lens.

These and other aspects and attributes of the present invention will be discussed with reference to the following drawings and accompanying specification.

## BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 is a diagram of the Ocular Stimulation Device (OSD) and the eye of a wearer of the device.

FIG. 2 is a diagram of the OSD applied to the eye, with stimulating photodiodes in contact with the cornea and the return electrodes in contact with the sclera or the eyelid.

FIG. 3 is a cross-section diagram of the OSD as it sits in contact with the eye. The stimulating photodiodes are in contact with the cornea and the return electrodes contact with the sclera or the eyelid.

FIG. 4 is a diagram of the Electrical Fields induced by the OSD.

FIGS. 5a and 5b are a plan view and an isometric view respectively of the OSD.

FIG. 6 is a diagram of a pair of stimulating glasses with stimulating LEDs.

FIG. 7 is a diagram of the stimulating glasses worn by a patient.

FIG. 8 is a diagram of the OSD worn by a patient also wearing the stimulating glasses.

FIG. 9 is a schematic representation of a cross-section of the stimulating photodiodes.

FIGS. 10a-10c show a cross-sectional view of molds used in creating the contact lens OSD and the embedded photonic devices and return electrodes.

FIGS. 11a and 11b are an isometric view of the male and female molds used in manufacturing the contact lens OSD.

FIGS. 12a-12c show a schematic of the circuit produced by the OSD in contact with the eye.

FIGS. 13a-13c show a schematic of the effective circuit produced by the OSD with different wavelengths of light used.

FIGS. 14a-14c show a schematic of the effective circuit produced by the OSD in a biphasic, anodic/cathodic (A/C) arrangement. Anodic and cathodic stimulation are produced by different wavelengths of light.

FIG. 15 is a diagram showing the effective input waveforms and resulting stimulation waveforms for a single pole (either anodic or cathodic).

FIG. 16 is a diagram showing the effective input waveforms and resulting stimulation waveforms for a biphasic, A/C device and the resulting anodic and cathodic stimulation waveforms.

FIG. 17 is a block diagram of the circuitry used in controlling the stimulating LEDs in the stimulating glasses.

## DETAILED DESCRIPTION OF THE INVENTION

While this invention is susceptible of embodiment in many different forms, there is shown in the drawing, and will be described herein in detail, specific embodiments thereof with the understanding that the present disclosure is to be considered as an exemplification of the principles of the invention and is not intended to limit the invention to the specific embodiments illustrated.

A preferred embodiment of the present invention provides an ocular stimulation device (OSD) **5** having a stimulating contact lens **10** to be worn on the exterior of an eye **12** and makes an electrical contact with the eye **12**. Referring to FIG. 1, the contact lens **10** is a clear, flexible, lens; embedded in the lens are stimulating photodiodes **16** and return electrodes **18**, which generate an electric field **20** within the eye **12** as shown in

FIG. 4. The generation of an electric field **20** provides a therapeutic rescue effect of the remaining visual pathway. The resulting effect is an overall improvement in vision loss and prevents or slows the further progression of Retinal Degeneration or other types of ocular disease.

The OSD **5**, when properly placed on the eye **12** as in FIG. 2, has the stimulating photodiode **16** forming an electrical contact with the cornea **22** of the eye **12**. The return electrodes **18** make an electrical contact with either the sclera **24** of the eye **12** or with an eyelid **26** of a wearer (FIG. 3).

The stimulating photodiodes **16** are shown positioned on a central portion of the OSD **5**, having two arcuate shaped electrodes **30** dimensioned to border and contact a peripheral portion of the cornea **22**. The return electrodes **18** has an axially extending portion **32** connecting to the photodiodes **18** and a circumferentially extending portion **34** for contacting the sclera or eyelid or both as seen in FIG. 5.

The OSD **5** provides electrical stimulation to the eye when activated by the electromagnetic radiation or by inductance effect. In a preferred form, a pair of stimulating eye glasses **36** of FIG. 6 provide electromagnetic radiation to the OSD **5**. A user or wearer **38**, as seen in FIGS. 7 and 8, wears the stimulating glasses **36** which have a frame **39** embedded with light emitting diodes (LED) **40** or another form of light producing elements, and filtered lenses **41**. Control circuitry **45** is attached to the frame and preferably in a discrete location as shown in FIG. 8 The LEDs **40** are used in a preferred embodiment and are chosen to provide a certain wavelength of light **43** to which the stimulating photodiodes **16** embedded in the OSD **5** are tuned, and to which the lenses 41 filter.

Specifically, in one embodiment of the invention, the glasses **36** are produced with a low pass lens, a lens that will pass through the entire visible spectrum and reflect the near infrared (NIR) and infrared (IR) wavelengths. In one preferred form, the stimulating photodiodes **16** are chosen to emit a wavelength in the range of 740 - 1000 nm and more preferably of 880 nm. The stimulating photodiodes **16** on the OSD **5** are tuned to respond to the 880 nm wavelength and produce an electric charge upon incident of that wavelength of light.

FIG. 9 shows a preferred embodiment of the stimulating photodiode **16** as a PiN photodiode. The PiN electrode can be fabricated from well-known photoelectric materials, such as silicon, selenium, gallium arsenide, etc. The preferred embodiment utilizes a silicon based PiN photodiode.

The stimulating photodiode **16** is manufactured by standard silicon processing techniques. First, a selected N-type wafer **56** is thinned down to the appropriate

thickness **57**. In a preferred embodiment, the thickness is from about 5 μm to about 200 μm, more preferably from about 20 μm to 100 μm, and most preferably about 29 μm. A layer of silicon oxide is then deposited on the wafer. Metal contacts **54**, **55** are provided on opposite sides of the silicon wafer **56**. The wafer **56** is then patterned with standard lithography techniques, the silver oxide is etched, and the wafer **56** is doped with an appropriate p-type dopant **52**. Additional p+ dopants **54** and n-dopants **58** are applied to the areas of metal contact **54**, **55**. The wafer **56** is then coated with appropriate thickness of nitrides and oxides to produce an optical filter **62** responsive to the stimulating wavelength of light. The wafer is then patterned for metal coatings and a metal is applied and lifted off to develop the contacts **54** and **55**. The wafer **56** is once again patterned for removal from the wafer and the photodiodes are etched out of the wafer. The result after processing is a photodiode with the appropriate thickness, electrical responsitivity to certain wavelengths of light and with the appropriate shape to be embedded into the contact lens.

The OSD **5** is manufactured by standard ophthalmic lens techniques using glass or more preferably polymeric materials including substituted and unsubstituted acrylic acid polymers and copolymers and ester and anhydride derivative thereof. Suitable polymers include, but are not limited to, polymethyl methacrylate (PMMA), cellulose acetate butyrate (CAB), polycon, styrene, silicone acrylate, flourosilicone acrylate, carbosifocon, or hydrogel. The contact lens can be fabricated using any technique, such as machining, spin casting or mold casting. A preferred embodiment utilizes a heat cured PMMA process in a cast mold. The PMMA material is inserted into a molding cavity such as that illustrated in FIGS. 10a-10c. When the two mold dies, the concave and convex components are mated together and result in a space relative to the thickness of the lens. The mold can be made to alter the optical properties of the lens and thus also correct for vision.

The convex mold **70** has reliefs **72** etched in it as illustrated in FIG. 11, which correspond to the shape of the manufactured stimulating photodiode. The concave mold **74** is etched with a corresponding relief **76** for the return electrode. The photodiodes are loaded into the convex mold **70** and the return electrode is loaded into the concave mold **74**. The PMMA or other material is then placed into the concave mold **74**. The convex mold **70** is mated with the concave mold **74**. The mated die **78** (FIG. 10b) is then heated to the appropriate temperature allowing for the PMMA to cure. Once cured, the molds are separated and the cured PMMA with semiconductor photodiodes is released. The result is the OSD **5**, a contact lens with embedded photodiode stimulation electrodes.

FIG. 12 shows a photodiode for responding to a single wavelength. FIGS. 13 and 14 show a photodiode for responding to two different wavelengths.

The photodiodes **16** can be arranged in any number of configurations as shown, for example, in FIGS. 12, 13 and 14. Further, the arrangement of photodiodes is not limited to the number of stimulating photodiodes. As few as one stimulating photodiodes can be used and any combination of shunt, parallel (FIGS. 12a, 13a, 14a) or combination of shunt and parallel (FIGS. 12b, 13b, 14b) or other series arrangements can be utilized as well.

Further, the photodiodes can be arranged in such a manner as to provide a bi-phasic, A/C stimulation by arranging the diodes in an inverse manner as in FIG. 14. In this embodiment, the two photodiodes are tuned to different wavelengths of light and only provide electrical stimulation when excited by that specific wavelength of light.

In a preferred embodiment, a first photodiode (LED 1) is tuned to 880 nm and a second photodiode (LED 2) is tuned to 940 nm (FIG. 13). When a stimulation light pattern with a wavelength of 940 nm strikes the OSD **5**, one side of the OSD **5** will be stimulated and produce a cathodic stimulation. When a stimulation light pattern of 880 nm wavelength strikes the OSD **5**, an anodic stimulation occurs. The resulting stimulation is seen in FIG. 16. When LED 1 shines on the OSD **5** with no light from LED 2, then there is a cathodic stimulation. When LED 2 shines on the OSD **5** with no light from LED 1, then there is an anodic stimulation. When there is light from both LED 1 and LED 2, the two stimulation patterns cancel each other, achieving the same stimulation as with no light.

When the OSD **5** is arranged in a manner such as in FIG. 12, then a single wavelength of light **30** will produce the stimulation pattern as in FIG. 15. This same pattern can also be achieved without the use of the stimulation glasses **36**.

The present invention further contemplates tuning the stimulating photodiodes to ambient lighting conditions so that the eye glasses **36** and photodiodes **40** are not required in this embodiment.

The effective result of stimulating the eye **12** is an electric field **20** generated in the eye **12**. Another embodiment for the OSD **5** is a method for delivering an electric field **20** to release a predisposed drug such as in iontophoresis.

FIG. 17 shows the control circuit **45** has a microprocessor **80** with input controls **82**, display circuitry **84**, a display **86**, and switches **88** for activating LED1 and LED2.

It should be understood that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of

the present invention and without diminishing its intended advantages. It is therefore intended that such changes and modifications be covered by the appended claims.